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Rhabdoid Tumor of the Kidney: A Report of Two Cases With Respective Tumor Markers and a Specific Chromosomal Abnormality, del(11p13)

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Malignant rhabdoid tumor is a rare, aggressive, invariably lethal tumor that is resistant to multimodal treatment. In this report, two patients with malignant rhabdoid tumor of the kidney (RTK) are described. The first patient is the first case of RTK with hyperreninemia, and the second case is also the first case with a specific chromosomal abnormality, del 11p13. The first patient presented with hematuria and a mass in the left kidney. Plasma renin, angiotensin, and aldosterone levels were elevated and paralleled the tumor progression. The karyotype of the tumor cells was normal (46,XX). In the second patient, who presented with a mass in the right kidney, the concentration of plasma tissue polypeptide antigen was elevated and paralleled the tumor progression. The karyotype of the tumor cells was 46,XX, del(11)(pter-p13::p12-qter). RTK with a cytogenetic abnormality of del(11p13), which is usually found in aniridia-Wilms' tumor syndrome, has not been known. Both patients died of metastatic disease within 7 months of diagnosis in spite of the multimodal therapy.

The clinicopathology of RTK and the differences between Wilms' tumor and RTK raise compelling questions which should be the subject of future studies.

Key words: rhabdoid tumor of the kidney, del 11p13, hyperreninemia, tissue polypeptide antigen

INTRODUCTION

Malignant rhabdoid tumor of the kidney (RTK) was first identified in 1978 in the National Wilms' Tumor Study (NWTS) [1]. RTK, while representing only 2% of all childhood renal tumors, was segregated from Wilms' tumor and another sarcomatous variant of renal tumors, clear cell sarcoma of the kidney (CCSK) and anaplasia of the kidney (AK) [2–5]. Malignant rhabdoid tumor has been reported in various anatomic sites other than the kidney [6]. Now, consistently with this, various cellular origins have been proposed for malignant rhabdoid tumor [7].

Wilms' tumor is associated with a good prognosis. RTK, on the other hand, is highly aggressive, resistant to multimodal therapy, and often fatal [1,4,5]. Because RTK is so rare, little is known of its clinicopathology, and no treatment modality has been established in spite of a few attempts [8].

In this report, the clinicopathology and the results of the immunocytochemical study of two patients with RTK are presented. A patient with renin-producing RTK was presented for the first time in Case 1 and a patient with RTK-producing tissue polypeptide antigen (TPA) was demonstrated in Case 2. The tumor cells of Case 2 also showed, for the first time, a specific cytogenetic abnormality, deletion 11p13, which is usually found in aniridia-Wilms' tumor syndrome [9,10].

CASE REPORTS

Case 1

An 18-month-old female, the second child born to healthy, unrelated parents, presented with hematuria and a huge tumor of the left abdomen. Her past history was significant only for low birth weight (2,250 g). Laboratory examination on admission revealed anemia with a hemoglobin concentration of 8.6 g/dL and an elevated lactate dehydrogenase (LDH) of 1,090 IU/L. There was no evi-

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dence of aniridia, genitourinary abnormalities, mental retardation, or hemihypertrophy. Her blood pressure was elevated (138/70 mmHg). The plasma renin (8.5 ng/mL/hr), angiotensin 1 (1,500 pg/mL), angiotensin 2 (210 pg/mL), and aldosterone (450 pg/mL) concentrations were all elevated. The patient showed the electrolyte imbalance including hypokalemia (2.7 mEq/L). Her karyotype, determined from the peripheral lymphocytes, was normal (46,XX). Angiography revealed replacement of the left kidney by tumor. However, there was no stenosis of the vena cava or renal artery.

En block resection of the left kidney and the surrounding lymph nodes was performed. The kidney had dimensions of $8 \times 7 \times 4.5$ cm and weighed 154 g. The tumor was surrounded with normal tissue of the kidney for the most part but there was invasion of the inferior mesenteric artery and the periaortic lymph nodes. There was no distant metastasis.

After surgery, a combination therapy including vincristine, actinomycin-D, adriamycin, cyclophosphamide and irradiation (30 Gy) of the tumor bed was employed. The concentration of plasma renin, angiotensin 1, angiotensin 2, and aldosterone decreased immediately after the surgery.

At age 20 months, the patient developed multiple lung metastasis in spite of the continuous chemotherapy. Subsequently, at age 22 months, liver infiltration and bone marrow involvement became apparent. Renin-angiotensin-aldosterone concentrations increased in parallel with the tumor progression, although no metastasis to the contralateral kidney was confirmed. At age 23 months, the patient died. There was no cerebral metastasis during the clinical course.

Case 2

A 2-month-old female, born to healthy, unrelated parents, presented with a right abdominal tumor. There was no evidence of aniridia, hemihypertrophy, or hypertension. Laboratory examination revealed anemia with hemoglobin of 9.9 g/dL, and an elevated LDH (3,426 IU/L). The tumor marker TPA was markedly elevated (>1,500 ng/mL). The carcinoembryonic antigen (CEA) and alphafetoprotein were not elevated.

The tumor with dimensions of $9 \times 8 \times 5.5$ cm and weight of 230 g, which invaded the outer surface of renal capsule, renal vein outside of the kidney, and ureter, was completely resected. Metastasis to the para-aortic lymph nodes was recognized. No distant metastasis was recognized. Combination therapy consisting of chemotherapy with vincristine, actinomycin-D, cisplatin, adriamycin, and cyclophosphamide, and radiotherapy was performed. The TPA concentration temporarily decreased to near negative levels. However, paralleled with a sudden increase in TPA concentration, metastases to lung, liver, and bone marrow were discovered at age 8 months. At age 9 months, the patient died of the tumor progression to pleuritis and peritonitis carcinomatosa. There was no cerebral metastasis during the clinical course.

Autopsies were not done in either patient.

METHODS

Chromosome Analysis

The tumor cells were treated with 0.02 μg/mL colcemide for 2 hr. Hypotonic treatment was carried out with 0.075 M KCl for 15 min. The preparations were fixed with methanol-acetic acid (3:1, v/v). The karyotype was analyzed with ordinary G banding.

Immunocytochemistry

The samples suspended in the medium RPMI-1640 were seeded on slides, fixed in −20°C cold acetone, and air-dried. The samples were stained with the indirect immunofluorescence method using the first antibodies and subsequently FITC-labeled second antibodies. The first antibodies used were anti-α_1 integrin (rabbit, Chemicon, Temecula, CA), anti-α_3 integrin (rabbit, Chemicon), anti-α_5 integrin (rabbit, Chemicon), anti-β_1 integrin (rabbit, Chemicon), anti-TGF-β (rabbit, King, Tokyo, Japan), anti-TGF-β-receptor type II (rabbit, Santa Cruz, Gebuhren Frei, Germany), anti-CDK2 (rabbit, Santa Cruz), anti-human collagen (I) (rabbit, Chemicon), anti-human laminin (rabbit, Chemicon), anti-keratin (rabbit, Dako, Carpenteria, CA), anti-vimentin (mouse monoclonal, Boehringer, Mannheim, Germany), and anti-desmin (mouse monoclonal, Boehringer, Germany). The second antibodies were FITC-labeled anti-rabbit IgG (gout, Dako) or FITC-labeled anti-mouse IgG (rabbit, Dako). Positive immunofluorescence was observed in Nikon fluorescence microscopy (Nikon, Tokyo, Japan).

RESULTS

Histopathology

The tumor tissue from the two patients was fixed and stained with haematoxillin and eosin. In both cases, the tumor consisted of round to oval cells with an abundant cytoplasm and prominent nucleoli. There was fine, granular eosinophilic material in the cytoplasm of many of the cells (Fig. 1a,b). These findings are characteristic of RTK.

Chromosome Analysis

The karyotype of the tumor cells from Case 1 was normal (46,XX). In Case 2, the karyotype of the tumor cells obtained from the ascites was 46,XX,del(11)(pter-p13::p12-qter) (Fig. 2).

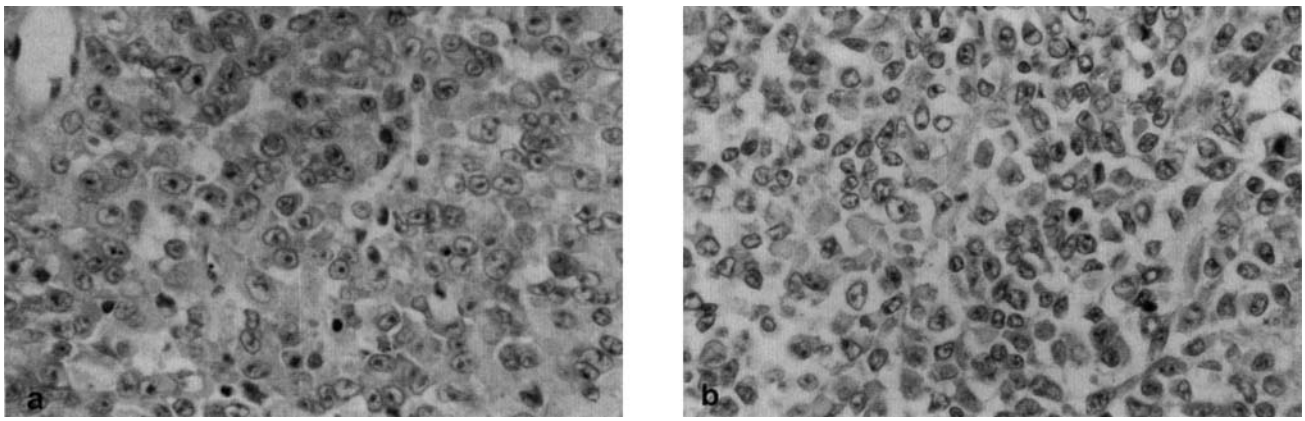

Fig. 1. **a:** Photomicrograph of a malignant rhabdoid tumor of the kidney (Case 1). Note the round to oval tumor cells with abundant cytoplasm and eccentric nuclei with prominent nucleoli. Several of the cells have acidophilic substance in the cytoplasm. **b:** Photomicrograph of a malignant rhabdoid tumor of the kidney (Case 2). Note the round to oval tumor cells with abundant cytoplasm and eccentric nuclei with prominent nucleoli. Most of the cells have acidophilic substance in the cytoplasm.

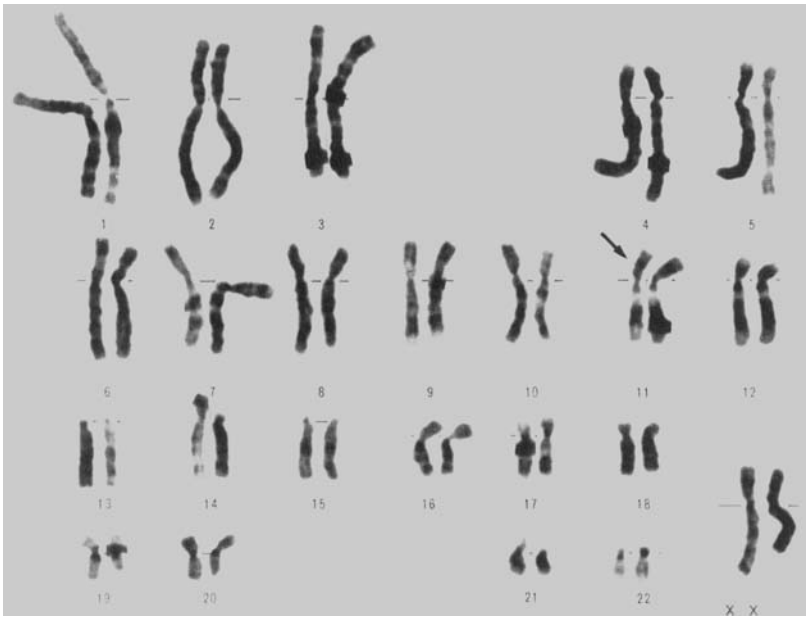

Fig. 2. Karyotype in Case 2 showing deletion of p13 to p12 on chromosome 11.

Immunocytochemistry

The samples from both patients showed a similar reaction pattern: negative for anti-keratin, anti-desmin, and anti-TGF-β, but positive for anti-vimentin, anti-laminin, and another antibodies.

DISCUSSION

Malignant rhabdoid tumor has been reported in various anatomic sites other than the kidney, such as the central nervous system, liver, chest wall, neck, pelvis, thymus, heart, extremities, back, and paravertebral region [11–16]. In addition, various cellular origins have been proposed for malignant rhabdoid tumor, such as neuroectodermal, myogenic, histiocytic, neural, epidermal, and metanephric-blastemal [17–22]. In spite of its immunohistologic characteristics, the histogenesis of malignant rhabdoid tumor is still unclear, although metanephrogenic blastemal differentiation common to Wilms' tumor and RTK has been described in a few cases [23,24].

Consistent with the various anatomic sites and cellular origins, various substances such as tumor marker have been reported. They are tissue polypeptide antigen [24], parathyroid hormone-related protein [25], insulin-like growth factor II [26]. However, the use of tumor markers in the diagnosis of RTK is not widely accepted [27]. In Case 1, there were elevations of plasma renin, angiotensin, and aldosterone concentrations. High levels of renin, angiotensin, and aldosterone can be caused by heart failure, renal failure, reno-vascular hypertension, and stenosis of the renal artery after irradiation [28–31]. Because there was no status which can cause hyperreninemia except the tumor, and the plasma levels paralleled the tumor progression, the elevation of renin, angiotensin, and aldosterone was suggested to be the result of tumor production. Although the presence of renin-producing Wilms' tumor has been known [32,33], there was no report of renin-producing RTK. In Case 2, TPA was detected in the plasma. TPA is thought to be an epithelial marker which is usually detected in Wilms' tumor and the developing kidney [10,24].

A first clue to the etiology of Wilms' tumor was discovered by Riccardi et al. [9] who reported the aniridia-Wilms' tumor association and the deletion of 11p13. It is now suspected that the tumor suppressor genes, WT-1 of 11p13 [34], WT-2 of 11p15 [35], p53 of 17p13 [36], and loss of heterozygosity of 16q [37], are related to the development of Wilms' tumor. The linkage of tumor suppressor genes and a physical complex WT-1 with p53 protein contribute to the ability of WT-1 to repress the transcription of potential target genes [38]. These results have come from the study of Wilms' tumor, not sarcomatous tumors of the kidney. The specific abnormal karyotype of t(11:22) and del(3)(q21) for RTK was reported [39,40]. However, to the best of our knowledge, the deletion 11p13 is not present in any other reported karyotype of RTK. The deletion of 11p13 in Case 2 indicates that there may be similar mechanisms of oncogenesis for RTK and Wilms' tumor. The differences between Wilms' tumor and the other types of renal tumors including RTK raise compelling questions which should be the subject of future studies.

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